Welcome to STN International! Enter x:x

LOGINID: ssptacmb1647

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

```
NEWS
                 Web Page URLs for STN Seminar Schedule - N. America
                 "Ask CAS" for self-help around the clock
NEWS 2
NEWS 3 FEB 27
                 New STN AnaVist pricing effective March 1, 2006
NEWS 4 MAY 10 CA/Caplus enhanced with 1900-1906 U.S. patent records
NEWS 5 MAY 11
                 KOREAPAT updates resume
                 Derwent World Patents Index to be reloaded and enhanced
NEWS 6 MAY 19
NEWS 7
         MAY 30
                 IPC 8 Rolled-up Core codes added to CA/CAplus and
                 USPATFULL/USPAT2
NEWS 8
         MAY 30
                 The F-Term thesaurus is now available in CA/CAplus
         JUN 02
                 The first reclassification of IPC codes now complete in
NEWS
                 INPADOC
                 TULSA/TULSA2 reloaded and enhanced with new search and
NEWS 10
         JUN 26
                 and display fields
NEWS 11 JUN 28
                 Price changes in full-text patent databases EPFULL and PCTFULL
NEWS 12 JUL 11
                 CHEMSAFE reloaded and enhanced
                 FSTA enhanced with Japanese patents
NEWS 13 JUL 14
                 Coverage of Research Disclosure reinstated in DWPI
NEWS 14 JUL 19
                 INSPEC enhanced with 1898-1968 archive
NEWS 15 AUG 09
NEWS 16 AUG 28 ADISCTI Reloaded and Enhanced
                 CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 17
         AUG 30
NEWS 18
         SEP 11
                 CA/CAplus enhanced with more pre-1907 records
                 CA/CAplus fields enhanced with simultaneous left and right
NEWS 19
         SEP 21
                 truncation
                 CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 20
         SEP 25
                 CAS REGISTRY(SM) no longer includes Concord 3D coordinates
         SEP 25
NEWS 21
                 CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 22
         SEP 25
         SEP 28
                 CEABA-VTB classification code fields reloaded with new
NEWS 23
                 classification scheme
```

NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

```
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8
NEWS X25 X.25 communication option no longer available
```

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

=> file medline embase biosis caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

0.21 0.21 FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 13:32:25 ON 05 OCT 2006

FILE 'EMBASE' ENTERED AT 13:32:25 ON 05 OCT 2006 Copyright (c) 2006 Elsevier B.V. All rights reserved.

FILE 'BIOSIS' ENTERED AT 13:32:25 ON 05 OCT 2006

Copyright (c) 2006 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 13:32:25 ON 05 OCT 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

=> s (methotrexate or methotrexate(w)triglutamate) and (prostate(w) specific(w) membrane(w) antigen or PMSA)

33 (METHOTREXATE OR METHOTREXATE(W) TRIGLUTAMATE) AND (PROSTATE(W)

SPECIFIC(W) MEMBRANE(W) ANTIGEN OR PMSA)

=> dup rem

ENTER L# LIST OR (END):11

PROCESSING COMPLETED FOR L1

24 DUP REM L1 (9 DUPLICATES REMOVED)

=> dis ibib abs 12 10-24

ANSWER 10 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:182244 CAPLUS

DOCUMENT NUMBER:

140:223261

TITLE:

Polymeric delivery systems

INVENTOR(S):

Griffiths, Gary L.; Goldenberg, David M.; Hansen, Hans

J.

PATENT ASSIGNEE(S):

Immunomedics, Inc., USA

SOURCE:

U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S.

Ser. No. 209,592.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE					
	<del>-</del>								
US 2004043030	A1	20040304	US 2003-456580	20030609					
US 2003026764	A1	20030206	US 2002-209592	20020731					
CA 2455856	AA	20030213	CA 2002-2455856	20020731					
EP 1411987	A2	20040428	EP 2002-749088	20020731					
R: AT, BE, CH,	DE, DK	, ES, FR, G	GB, GR, IT, LI, LU,	NL, SE, MC, PT,					
IE, SI, LT,	LV, FI	, RO, MK, C	CY, AL, TR, BG, CZ,	EE, SK					
JP 2005501052	T2	20050113	JP 2003-516572	20020731					
PRIORITY APPLN. INFO.:			US 2001-308605P	P 20010731					
			US 2002-209592	A2 20020731					
			WO 2002-GB3494	W 20020731					

The present invention relates to a method of targeting an agent towards a AB targeting site in a tissue comprising administering a multi-specific antibody or antibody fragment comprising a targeting arm and a capture arm that binds to a polymer conjugate, and administering a polymer conjugate

to the tissue. The present invention also relates to a kit for targeting a target site within a comprising a multi-specific antibody or antibody fragment comprising a targeting arm and a capture arm that binds to a polymer conjugate, and a polymer conjugate.

L2 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:141669 CAPLUS

DOCUMENT NUMBER:

140:216171

TITLE:

Anti-PSMA antibodies and PSMA multimers for diagnosis, prognosis and therapy of prostatic or non-prostatic

Panaora

INVENTOR(S):

Maddon, Paul J.; Donovan, Gerald P.; Olson, William C.; Schulke, Norbert; Gardner, Jason; Ma, Dangshe

PATENT ASSIGNEE(S):

USA

SOURCE:

U.S. Pat. Appl. Publ., 151 pp., Cont.-in-part of Appl.

No. PCT/US02/33944.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'					KIND DATE					ICAT							
US								0219			003-					0030	321
	2003												20021023				
	2003																
							20040513										
WO	WO 2003034903 B1 W: AE, AG, AL, AM,								ъΔ.	BB	BG	BR	ВV	B7.	CA	CH.	CN.
	w:																
							DK,										
							IN,										
							MD,										
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TN,	TR,	TT,	TZ,
	UA, UG, US, UZ,					VN,	YU,	YU, ZA, ZW									
	RW:	GH,	·GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
		KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	ΕĖ,	ES,
							IT,										
							GQ,										
US	2004														2	0031	027
	2005																
PRIORIT											001-						
FRIORII	I ALL	LILY.	1111	• •							002-				P 2		
											002-						
											1002-1						
											003-		_				
										US 2	003-	6956	67		A2 2	0031	027

- AB The invention includes antibodies or antigen-binding fragments thereof which bind specifically to conformational epitopes on the extracellular domain of prostate specific membrane antigen (PSMA), compns. containing one or a combination of such antibodies or antigen-binding fragments thereof, hybridoma cell lines that produce the antibodies, and methods of using the antibodies or antigen-binding fragments thereof for cancer diagnosis and treatment. The invention also includes oligomeric forms of PSMA proteins, compns. comprising the multimers, and antibodies that selectively bind to the multimers.
- L2 ANSWER 12 OF 24 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER:

2005428234 EMBASE

TITLE:

Targeting prostate-specific

membrane antigen in cancer therapy: Can

molecular medicine be brought to the surface?.

AUTHOR:

Leach F.

F. Leach, Scott Department of Urology, Baylor College of CORPORATE SOURCE:

Medicine, 6560 Fannin, Houston, TX 77030, United States.

fleach@bcm.tmc.edu

Cancer Biology and Therapy, (2004) Vol. 3, No. 6, pp. SOURCE:

> 559-560. . Refs: 12

ISSN: 1538-4047

COUNTRY:

United States

DOCUMENT TYPE:

Journal; General Review

FILE SEGMENT:

016 Cancer

028 Urology and Nephrology 037 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE:

English

ENTRY DATE:

Entered STN: 27 Oct 2005

Last Updated on STN: 27 Oct 2005

Systemic chemotherapy can be associated with significant morbidity as a AB result of non-specific side effects and drug toxicity. A major advance in cancer therapy is the ability to target specific molecules and pathways due to increased knowledge of gene expression and biochemical function. In this issue of Cancer Biology & Therapy, a targeted approach to prostate cancer chemotherapy is explored using the inherent enzymatic activity of prostate-specific membrane antigen

(PSMA) and peptide conjugated methotrexate. Substrate specificity and specific activity were determined using soluble PSMA while selective drug toxicity was determined using clonal inhibition of PSMA+ and PSMA- cancer cell lines. Peptide conjugates linked to methotrexate were identified with enhanced selective clonal inhibition in the presence of PSMA. Despite these promising results, multiple variables affecting clinical feasibility such as substrate stability and non-PSMA dependent drug uptake will require careful consideration before PSMA is ready for prime time as a selective chemotherapeutic target. .COPYRGT.2004 Landes Bioscience.

MEDLINE on STN ANSWER 13 OF 24

DUPLICATE 2

ACCESSION NUMBER: DOCUMENT NUMBER:

MEDLINE 2004418666 PubMed ID: 15044850

TITLE:

Use of methotrexate-based peptide substrates to characterize the substrate specificity of prostate

-specific membrane antigen

(PSMA).

**AUTHOR:** 

Mhaka Annastasiah; Gady Alyssa M; Rosen D Marc; Lo

Kin-Ming; Gillies Steven D; Denmeade Samuel R

CORPORATE SOURCE:

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, The Johns Hopkins School of Medicine, Baltimore,

Maryland, USA.

SOURCE:

Cancer biology & therapy, (2004 Jun) Vol. 3, No. 6, pp.

551-8. Electronic Publication: 2004-06-10. Journal code: 101137842. ISSN: 1538-4047.

PUB. COUNTRY:

United States

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

200505

ENTRY DATE:

Entered STN: 25 Aug 2004

Last Updated on STN: 20 May 2005 Entered Medline: 19 May 2005

Prostate-Specific Membrane Antigen AB

(PSMA) is a glutamate carboxypeptidase II that is highly expressed by both normal and malignant prostate epithelial cells and by the neovasculature of many tumor types but is not expressed by endothelial cells in normal PSMA possesses the hydrolytic properties of an N-acetylated alpha-linked acidic dipeptidase (NAALADase) and also functions as a pteroyl poly-gamma-glutamyl carboxypeptidase (i.e., folate hydrolase).

Therefore, PSMA can be targeted for activation of peptide-based prodrugs within the extracellular fluid of prostate cancers. In this study, methotrexate-based peptide analogs were evaluated to identify PSMA selective substrates that are also stable to nonspecific hydrolysis in human and mouse plasma. These methotrexate analogs were also characterized for in vitro toxicity against PSMA and nonPSMA producing human cancer cell lines. Analogs containing gamma-linked glutamate residues were most efficiently hydrolyzed by PSMA, but were unstable in plasma. Analogs containing both alpha- and gamma-linked acidic amino acids were less efficiently hydrolyzed by PSMA but were most stable in plasma. Analogs were 5-10 fold more selectively toxic in vitro in the presence of active PSMA. These studies have identified PSMA selective, plasma stable peptide substrates that can be incorporated into prodrugs targeted for activation by PSMA within prostate cancer sites.

ANSWER 14 OF 24 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights L2 reserved on STN

2004383856 EMBASE ACCESSION NUMBER:

Genetic modification of T cells for cancer therapy. TITLE:

Imai C.; Campana D. AUTHOR:

CORPORATE SOURCE: Dr. D. Campana, Department of Hematology-Oncology, St. Jude

> Children's Research Hosp., 332 North Lauderdale, Memphis, TN 38105-2794, United States. dario.campana@stjude.org

Journal of Biological Regulators and Homeostatic Agents, SOURCE:

(2004) Vol. 18, No. 1, pp. 62-71. .

Refs: 109

ISSN: 0393-974X CODEN: JBRAER

COUNTRY: Italy

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer

Human Genetics 022 Pharmacology 030

Immunology, Serology and Transplantation 026

Drug Literature Index 037

039 Pharmacy

English LANGUAGE: SUMMARY LANGUAGE: English

Entered STN: 24 Sep 2004 ENTRY DATE:

Last Updated on STN: 24 Sep 2004

The use of immune cells with restricted specificities for the treatment of AB cancer is a rapidly emerging area of clinical research. Chimeric receptors composed of the single-chain variable domain of murine antibodies and human signaling molecules are a promising tool to redirect the specificity of autologous or allogeneic immune cells. The success of this approach depends on the identification of target molecules expressed preferentially on cancer cells. Moreover, appropriate primary and sedondary stimuli must be delivered to generate vigorous and durable immune responses. Since cancer cells often lack ligands for key co-stimulatory molecules, the addition of molecules such as CD28 or 4-1BBto the chimeric receptors can significantly improve their function. Studies in vitro and in animal models indicate that immune cells expressing chimeric receptors can have remarkable anti-cancer activity, while experimental and clinical data indicate that long-term persistence of adoptively transferred cells is feasible. Therefore, testing of this approach in clinical trials is warranted. We here review the principles and methodologies for designing chimeric receptors and delivering them into immune cells, as well as some of the potential complications associated with this form of cell therapy. .COPYRGT. Wichtig Editore, 2004.

ANSWER 15 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN L2

ACCESSION NUMBER: 2003:335142 CAPLUS

138:348687 DOCUMENT NUMBER:

Use of selective tissue vascular thrombogens for TITLE:

targeting tumor tissues

INVENTOR(S):

Liu, Cheng; Edgington, Thomas S.

PATENT ASSIGNEE(S):

Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.; The

Scripps Research Institute

SOURCE:

PCT Int. Appl., 100 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.				
WO 2003035688	A2 20030501	WO 2002-EP11925	20021024			
WO 2003035688	A3 20040318					
W: AE, AG, AL,	, AM, AT, AU, AZ,	BA, BB, BG, BR, BY, B	BZ, CA, CH, CN,			
		DZ, EC, EE, ES, FI, C				
		KE, KG, KP, KR, KZ, I				
		NZ, OM, PH, PL, PT, I				
SI, SK, TJ	, TM, TN, TR, TT,	UA, UZ, VC, VN, YU,	ZA, ZW			
RW: AM, AZ, BY	, KG, KZ, MD, RU,	TJ, TM, AT, BE, BG, C	CH, CY, CZ, DE,			
DK, EE, ES	, FI, FR, GB, GR,	IE, IT, LU, MC, NL,	PT, SE, SK, TR			
		AU 2002-350623				
US 2003194400	A1 20031016	US 2002-279733	20021024			
EP 1443954	A2 20040811	EP 2002-785305	20021024			
R: AT, BE, CH	, DE, DK, ES, FR,	GB, GR, IT, LI, LU, I	NL, SE, MC, PT,			
		CY, AL, TR, BG, CZ, 1	EE, SK			
PRIORITY APPLN. INFO.:	•	US 2001-336331P	P 20011026			
		US 2002-412194P	P 20020920			
		WO 2002-EP11925	W 20021024			
an mile decreased an access		mothoda to initiato s	ite-specific			

The invention provided compns. and methods to initiate site-specific AΒ thrombosis in tumor vasculature. The invention particularly provides Selective Tissue Vascular Thrombogens (STVTs) that can targeted thrombosis, infarction and destruction of selected tissues, for example, tumors. The present invention also provides methods for using the disclosed compns. and methods to treat tumors.

ANSWER 16 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: DOCUMENT NUMBER:

2003:334823 CAPLUS

138:352761

TITLE:

Anti-prostate specific

membrane antigen (PSMA) antibodies

and fragments for cancer diagnosis and therapy and

antitumor screening

INVENTOR(S):

Maddon, Paul J.; Donovan, Gerald P.; Olson, William C.; Schuelke, Norbert; Gardner, Jason; Ma, Dangshe

PATENT ASSIGNEE(S):

PSMA Development Company, L.L.C., USA

SOURCE:

PCT Int. Appl., 238 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	CENT :	NO.			KIND DATE					APPL:	DATE						
			<b>-</b>			-						<del>-</del>	<del>-</del>		-		
WO 2003034903 A2							2003	20030501 WO 2002-US33944 2002									
WO	2003	0349	03		<b>A</b> 3		2003	1030									
WO 2003034903				B1 20040513													
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		co,	CR,	CU,	CZ,	DE,	DK,	DM,	DΖ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KΕ,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,
		LS,	LT,	·LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
		PL.	PT.	RO.	RU.	SD.	SE.	SG,	SI,	SK,	SL,	TJ,	TM,	TN,	TR,	TT,	TZ,

```
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                                                   20021023
    CA 2464239
                         AΑ
                                20030501
                                           CA 2002-2464239
                                           EP 2002-802198
    EP 1448588
                         A2
                                20040825
                                                                   20021023
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
    JP 2005523683
                         T2
                                20050811
                                            JP 2003-537481
                                                                   20021023
                                20040219
                                            US 2003-395894
                                                                   20030321
    US 2004033229
                         A1
    US 2004161776
                         A1
                                20040819
                                            US 2003-695667
                                                                   20031027
                                20050929
                                            US 2004-976352
                                                                   20041027
    US 2005215472
                         Al
PRIORITY APPLN. INFO.:
                                            US 2001-335215P
                                                                Р
                                                                  20011023
                                            US 2002-362747P
                                                                Р
                                                                   20020307
                                            US 2002-412618P
                                                                Р
                                                                   20020920
                                            WO 2002-US33944
                                                                W
                                                                  20021023
                                            US 2003-395894
                                                                A2 20030321
                                            US 2003-695667
                                                                A2 20031027
    The invention includes antibodies or antigen-binding fragments thereof
AΒ
    which bind specifically to conformational epitopes on the extracellular
```

domain of PSMA, compns. containing one or a combination of such antibodies or antibodies or antigen-binding fragments thereof, hybridoma cell lines that produce the antibodies, and methods of using the antibodies or antigen-binding fragments thereof for cancer diagnosis and treatment. invention also includes oligomeric forms of PSMA proteins, compns. comprising the multimers, and antibodies that selectively bind to the multimers.

ANSWER 17 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:242117 CAPLUS

DOCUMENT NUMBER: 138:276253

Methods and compositions for treating or preventing TITLE:

skin disorders using binding agents specific for

prostate specific membrane

antigen

Bander, Neil INVENTOR (S):

Cornell Research Foundation, Inc., USA PATENT ASSIGNEE(S):

PCT Int. Appl., 225 pp. SOURCE:

CODEN: PIXXD2

Patent DOCUMENT TYPE: English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	CENT 1	NO.								APPL	ICAT		DATE				
WO	2003	 0243	<b>-</b> 38		A2	A2 20030327			,	WO 2	 002-1						
WO	2003	0243	88		A3		2003	0731									
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
							IN,										
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,
							ZA,										
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
							TM,										
		GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,
		-					NE,										
CA	2452	288		•	AΑ	·	2003	0327	·	CA 2	002-	2452	288		2	0020	530
US	2003	1618	32		A1		2003	0828		US 2	002-	1605	06		2	0020	530
	1427															0020	530
							ES,									MC,	PT,
							RO,							•			

JP 2005527474 T2 20050915 JP 2003-528486 20020530 PRIORITY APPLN. INFO.: US 2001-324100P P 20010920 US 2002-362612P P 20020308 WO 2002-US17204 W 20020530

AB Methods and compns. for treating, preventing, or diagnosing epidermal or dermal disorders, e.g., psoriasis, are disclosed. The methods and compns. of the invention use binding agents, e.g., antibodies, specific for the extracellular domain of human prostate specific membrane antigen (PSMA).

L2 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:836381 CAPLUS

139:341719

DOCUMENT NUMBER: TITLE:

Use of bi-specific antibodies for pre-targeting

diagnosis and therapy

Immunomedics, Inc., USA

INVENTOR(S):

Goldenberg, David M.; Hansen, Hans J.; Leung, Shui-on;

McBride, William J.; Qu, Zhengxing

PATENT ASSIGNEE(S):

SOURCE:

U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of U.S.

Ser. No. 823,746.

CODEN: USXXCO

DOCUMENT TYPE: LANGUAGE: Patent English

17

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

1	PATENT NO.											ICAT:		DATE						
	 US	2003						2003	1023	US	2	 002-:	1506	 54		2	0020	517		
		70528				B1								19990823						
									20020117 US 2001-823746 20051108											
								2003	1127	CA	. 2	003-2		20030516						
	WO 2003097105 A1 2003112								1127	WO	2	003-0	GB21	10		20030516				
·		W:			AL,	AM,	AT,			BA, B							CH,	CN,		
										DZ, E										
										JP, K										
										MK, M										
			PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE, S	G,	SK,	SL,	ΤJ,	TM,	TN,	TR,	TT,		
										YU, Z										
		RW:								SL, S										
			KG,	ΚZ,	MD,	RU,	ТJ,	TM,	AT,	BE, B	G,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,		
										LU, M										
			BF,	ВJ,	CF,	CG,	CI,			GN, G						SN,	TD,	TG		
2	ΑU	2003	2279	39		A1				AU							0030			
]	ΕP	1506				A1				ΕP				0030						
		R:								GB, G								PT,		
			ΙE,	SI,	LT,	LV,	FI,			CY, A										
]	BR	2003	0100							BR							0030			
		1668				Α				CN										
	JР	2006	5063	25		T2				JF										
1	US	2005	0029	45		A1				US										
١	US	2006	0347	59		A1		2006				005-				_	0050			
						A1		2006	0629			005-				-	0050			
PRIOR	ITY	APP	LN.	INFO	.:							998-								
												998-					9981			
												999-				A2 1				
										US 2001-823746 US 1999-337756						A2 20010403 A2 19990622				
												999- 002-				A 20020517				
												002-				-				
פות	ጥኩ -		aon+	1	onti	0n ~	പ്പ		<u> </u>		_		-		W 20030516 z or antibody					

AB The present invention relates to a bi-specific antibody or antibody fragment having at least one arm that specifically binds a targeted tissue and at least one other arm that specifically binds a targetable construct.

The targetable construct comprises a carrier portion which comprises or bears at least one epitope recognizable by at least one arm of said bi-specific antibody or antibody fragment. The targetable construct further comprises one or more therapeutic or diagnostic agents or enzymes. The invention provides constructs and methods for producing the bi-specific antibodies or antibody fragments, as well as methods for using them.

ANSWER 19 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN L2

ACCESSION NUMBER:

2002:449519 CAPLUS

DOCUMENT NUMBER:

137:28278

TITLE:

Methods of treatment of angiogenesis-related disease

involving human MDA-7 protein

INVENTOR(S):

Chada, Sunil; Grimm, Elizabeth; Mhashilkar, Abner;

Schrock, Bob; Rajagopal, Ramesh

PATENT ASSIGNEE(S):

SOURCE:

University of Texas, USA PCT Int. Appl., 159 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PA.	rent 1	NO.			KIND DATE				1	APPL	ICAT		DATE					
						A2 20020613 A3 20040108				1	WO 2	001-	US47:	20011207					
		W:						AU,		BA,	BB,	ВG,	BR,	BY,	BZ,	CA,	CH,	CN,	
								DK,											
			GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚĖ,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	
								MD,											
			PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	
								ZA,											
		RW:						MZ,											
								TM,											
*								NL,				BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	
			GN,					NΕ,											
		2429				AA		2002											
		2002															0011		
		2002																	
	ΕP	1404						2004									0011		
		R:						ES,					Ll,	ъÚ,	ΝL,	SE,	MC,	PT,	
								RO,						• •		_	0077	007	
										JP 2002-547520									
PRIO	PRIORITY APPLN. INFO.:				. :					US 2000-254226P WO 2001-US47215									
				_ 7	-a +	<u> </u>	+·	h aa							W 20011207				

- The invention relates to gene therapy methods for the treatment of human AB disease. More specifically, the invention is directed to methods for treating a subject with an angiogenesis-related disease. In one embodiment, an adenoviral expression construct comprising a nucleic acid encoding a human MDA-7 protein under the control of a promoter operable in eukaryotic cells, is administered to said patient with a angiogenesis-related disease. The present invention thus provides for treatment of angiogenesis-related disease by through expression of mda-7 and inhibition angiogenesis. Such diseases include cancer.
- ANSWER 20 OF 24 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on L2 STN

ACCESSION NUMBER:

2001:404358 BIOSIS PREV200100404358

DOCUMENT NUMBER: TITLE:

Hydrolysis of methotrexate analogs by

prostate-specific membrane

antigen (PSMA).

Gady, Alyssa M. [Reprint author]; Rosen, D. Marc; Denmeade, AUTHOR(S):

Samuel R.

CORPORATE SOURCE:

SOURCE:

The Johns Hopkins School of Medicine, Baltimore, MD, USA Proceedings of the American Association for Cancer Research

Annual Meeting, (March, 2001) Vol. 42, pp. 230. print. Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research. New Orleans, LA, USA. March 24-28, 2001. American Association for Cancer

Research.

ISSN: 0197-016X.

DOCUMENT TYPE:

Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE:

English

ENTRY DATE:

Entered STN: 22 Aug 2001

Last Updated on STN: 22 Feb 2002

ANSWER 21 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:144870 CAPLUS

Synthesis of N-thiophosphonyl derivatives of glutamic TITLE:

acid

Dastgah, Azar; Lu, Haiyan; Mlodnosky, Karyn L.; Dinh, AUTHOR (S):

Trang T.; Berkman, Clifford E.

Dept. of Chemistry & Biochemistry, San Francisco State CORPORATE SOURCE:

Univ., San Francisco, CA, 94132, USA

Book of Abstracts, 217th ACS National Meeting, SOURCE:

Anaheim, Calif., March 21-25 (1999), CHED-397. American Chemical Society: Washington, D. C.

CODEN: 67GHA6

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE:

English Recently, it has been noted that increased intra- and extra-cellular levels of folate hydrolyzing enzymes (Gamma-Glutamyl Hydrolase, GGH; prostate specific membrane antigen,

PSM) are associated with tumor cell resistance to the antiproliferative drug methotrexate (MTX). Therefore, inhibitors of GGH or PSM could be therapeutically invaluable for combating MTX-resistant tumors by countering their mode of resistance. Initial studies indicated that traditional, phosphonamidate tetrahedral-intermediate analog inhibitors were unsuccessful against the target hydrolases. However, recent preliminary data has shown that the corresponding thiophosphonamidate analogs exhibit inhibitory activity against PSM and GGH. The synthesis of a limited series of these N-thiophosphonyl derivs. of glutamic acid will be presented.

MEDLINE on STN DUPLICATE 3 ANSWER 22 OF 24

ACCESSION NUMBER: 97330810 MEDLINE PubMed ID: 9187245 DOCUMENT NUMBER:

Structure of membrane glutamate carboxypeptidase. TITLE:

Rawlings N D; Barrett A J AUTHOR:

Department of Immunology, The Babraham Institute, CORPORATE SOURCE:

Cambridge, UK.

Biochimica et biophysica acta, (1997 May 23) Vol. 1339, No. SOURCE:

2, pp. 247-52.

Journal code: 0217513. ISSN: 0006-3002.

PUB. COUNTRY:

Netherlands

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

English LANGUAGE:

Priority Journals FILE SEGMENT:

199707 ENTRY MONTH:

Entered STN: 16 Jul 1997 ENTRY DATE:

Last Updated on STN: 3 Mar 2000 Entered Medline: 1 Jul 1997

Membrane glutamate carboxypeptidase (mGCP) hydrolyses pteroylpoly-gamma-AΒ glutamates, methotrexate tri-gamma-glutamate and N-acetyl-aspartyl-alpha-glutamate. The enzyme is thought to be required

for intestinal uptake of folate, for the resistance of some tumours to methotrexate, and for the metabolism of N-acetyl-aspartylglutamate, an abundant neuropeptide. It has recently been reported that mGCP is a protein also known as prostate-specific membrane antigen, homologous with transferrin receptor. This allows us to predict the domain structure of mGCP. Moreover, we have been able to assign the catalytic domain of mGCP to peptidase family M28, which contains cocatalytic zinc metallopeptidases. On the basis of the known structure of an aminopeptidase in family M28, we predict that Asp377, Asp387, Glu425, Asp453 and His553 are ligands of two atoms of zinc bound in the catalytic site of mGCP, and suggest that the aminopeptidases of Vibrio and Streptomyces can serve as valuable models in the design of inhibitors for this medically important enzyme.

ANSWER 23 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN

1997:738993 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 128:21580

Prostate-specific membrane TITLE:

antigen, a unique folate hydrolase: potential

target for prodrug therapy

Heston, Warren D. W.; Tong, W. P.; Pinto, J. T. AUTHOR(S):

Urologic Oncology Research Laboratory, Molecular CORPORATE SOURCE: Pharmacology and Experimental Therapeutics Section,

Sloan-Kettering Institute for Cancer Research, New

York, NY, USA

Molecular Urology (1997), 1(2/3), 215-219 SOURCE:

CODEN: MOURFE; ISSN: 1091-5362

Liebert PUBLISHER: DOCUMENT TYPE: Journal LANGUAGE: English

The aim of the current investigation was to determine whether prostate-specific membrane (PSM) antigen can be used as a prodrug target. In searching to identify the function of PSM antigen, we observed that it is a unique carboxypeptidase, which has hydrolytic activity with carboxy-terminal peptidic bonds involving glutamate. It is unique in that it will hydrolyze gamma- and alpha-linked peptides, such as the alpha linkage in N-acetylaspartylglutamate and the gamma-linked glutamates in polygammaglutamated folate or methotrexate. A substrate used to study the activity of PSM antigen is methotrexate trigammaglutamate. Because the trigammaglutamate is a poor substrate for transportation into the cell, we examined it as a potential prodrug form of this traditional anticancer drug. When we incubated it with LNCaP tumor cells, it was cytotoxic. We then incubated it with PC-3 cells that were or were not transfected with PSM antigen and found that it was cytotoxic to the PSM antigen-expressing cells. Polygammaglutamated folate antagonists should be considered for therapeutic approaches in prostate cancer.

THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 16 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DUPLICATE 4 ANSWER 24 OF 24 MEDLINE on STN

ACCESSION NUMBER: 1999035167

MEDLINE

DOCUMENT NUMBER:

PubMed ID: 9816319

TITLE:

Prostate-specific membrane

antigen: a novel folate hydrolase in human

prostatic carcinoma cells.

AUTHOR:

Pinto J T; Suffoletto B P; Berzin T M; Qiao C H; Lin S;

Tong W P; May F; Mukherjee B; Heston W D

CORPORATE SOURCE:

Nutrition Research Laboratory, Urology Research Laboratory, Pharmacology Analytical Laboratory, and George M. O'Brien Urology Research Center, Memorial Sloan-Kettering Cancer

Center, New York, New York 10021, USA.

CONTRACT NUMBER:

CA 08748-29 (NCI)

CA 39203 (NCI)

DK/CA 47650 (NIDDK)

+

SOURCE: Clinical cancer research : an official journal of the

American Association for Cancer Research, (1996 Sep) Vol.

2, No. 9, pp. 1445-51.

Journal code: 9502500. ISSN: 1078-0432.

PUB. COUNTRY:

United States

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

199902

ENTRY DATE:

Entered STN: 11 Mar 1999

Last Updated on STN: 3 Mar 2000 Entered Medline: 25 Feb 1999

A novel monoclonal antibody has been developed that reacts strongly with AΒ human prostatic cancer, especially tumors of high grade. This antibody (7E11C-5) is currently in Phase 3 trials as an imaging agent for metastatic disease. We have cloned the gene that encodes the antigen that is recognized by the 7EllC-5 monoclonal antibody and have designated this unique protein prostate-specific membrane (PSM) antigen. PSM antigen is a putative class II transmembranous glycoprotein exhibiting a molecular size of Mr 94,000. Functionally, class II membrane proteins serve as transport or binding proteins or have hydrolytic activity. Preliminary studies have demonstrated binding of pteroylmonoglutamate (folate) to membrane fractions that also cross-reacted with the PSM monoclonal antibody. We observed substantial carboxypeptidase activity as folate hydrolase associated with PSM antigen. The purpose of our study was to demonstrate that human prostatic carcinoma cells expressing PSM antigen exhibit folate hydrolase activity using methotrexate triglutamate (MTXGlu3) and pteroylpentaglutamate (PteGlu5) as substrates. Isolated membrane fractions from four human prostate cancer cell lines (LNCaP, PC-3, TSU-Prl, and Duke-145) were examined for folate hydrolase activity using capillary electrophoresis. After timed incubations at various pH ranges and in the presence and absence of thiol reagents, separation of pteroyl(glutamate)n derivatives was achieved with an electrolyte of sodium borate and SDS, while absorbance was monitored at 300 nm. The results demonstrate clearly that LNCaP cells, which highly express PSM, hydrolyze qamma-glutamyl linkages of MTXGlu3. The membrane-bound enzyme is an exopeptidase, because it progressively liberates glutamates from MTXGlu3 and PteGlu5 with accumulation of MTX and PteGlu1, respectively. The semipurified enzyme has a broad activity from pH 2.5 to 9.5 and exhibits activity maxima at pH 5 and 8. Enzymatic activity is maintained in the presence of reduced glutathione, homocysteine, and phydroxymercuribenzoate (0.05-0.5 mm) but was inhibited weakly by DTT (>/=0.2 mm). By contrast to LNCaP cell membranes, membranes isolated from other human prostate adenocarcinoma cells (PC-3, Duke-145, and TSU-Pr1) did not exhibit comparable hydrolase activity, nor did they react with 7E11-C5 monoclonal antibody. After transfection of PC-3 cells with a full-length 2.65-kb PSM cDNA subcloned into a pREP7 eukaryotic expression vector, non-PSM antigen-expressing PC-3 cells developed immunoreactivity to 7E11-C5 monoclonal antibody and demonstrated folate hydrolase activities and optimum pH activity profiles identical to those of LNCaP The membrane-bound enzymes from both LNCaP- and PC-3-transfected cells also have a capacity to hydrolyze an alpha-linked glutamyl moiety from N-acetyl-alpha-aspartylglutamate. We have identified that PSM antigen is a pteroyl poly-gamma-glutamyl carboxypeptidase (folate hydrolase) and is expressed strongly in human prostate cancer. Cancer cells that express this enzyme are resistant to methotrexate therapy. Those developing future therapeutic strategies in the treatment of prostate cancer that utilize folate antagonists need to consider this mechanism of resistance.

Welcome to STN International! Enter x:x

LOGINID: ssptacmb1647

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

```
Web Page URLs for STN Seminar Schedule - N. America
NEWS
     1
                 "Ask CAS" for self-help around the clock
NEWS
                New STN AnaVist pricing effective March 1, 2006
NEWS 3
        FEB 27
                 CA/CAplus enhanced with 1900-1906 U.S. patent records
        MAY 10
NEWS 4
                 KOREAPAT updates resume
        MAY 11
NEWS 5
                Derwent World Patents Index to be reloaded and enhanced
        MAY 19
NEWS
                 IPC 8 Rolled-up Core codes added to CA/CAplus and
        MAY 30
NEWS
    7
                 USPATFULL/USPAT2
                 The F-Term thesaurus is now available in CA/CAplus
        MAY 30
NEWS
     8
                 The first reclassification of IPC codes now complete in
         JUN 02
NEWS
    9
                 INPADOC
                 TULSA/TULSA2 reloaded and enhanced with new search and
         JUN 26
NEWS 10
                 and display fields
                 Price changes in full-text patent databases EPFULL and PCTFULL
NEWS 11
        JUN 28
                 CHEMSAFE reloaded and enhanced
NEWS 12 JUl 11
                 FSTA enhanced with Japanese patents
NEWS 13 JUl 14
                Coverage of Research Disclosure reinstated in DWPI
NEWS 14 JUl 19
                 INSPEC enhanced with 1898-1968 archive
NEWS 15 AUG 09
                 ADISCTI Reloaded and Enhanced
NEWS 16 AUG 28
                 CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 17
        AUG 30
                 CA/CAplus enhanced with more pre-1907 records
NEWS 18
        SEP 11
                 CA/CAplus fields enhanced with simultaneous left and right
         SEP 21
NEWS 19
                 truncation
NEWS 20
         SEP 25
                 CA(SM)/CAplus(SM) display of CA Lexicon enhanced
                 CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 21
         SEP 25
                 CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 22
         SEP 25
                 CEABA-VTB classification code fields reloaded with new
NEWS 23
         SEP 28
                 classification scheme
```

NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

```
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8
NEWS X25 X.25 communication option no longer available
```

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

FILE 'HOME' ENTERED AT 16:02:40 ON 05 OCT 2006

=> file medline embase biosis caplus

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST

0.42 0.42

FILE 'MEDLINE' ENTERED AT 16:04:04 ON 05 OCT 2006

FILE 'EMBASE' ENTERED AT 16:04:04 ON 05 OCT 2006 Copyright (c) 2006 Elsevier B.V. All rights reserved.

FILE 'BIOSIS' ENTERED AT 16:04:04 ON 05 OCT 2006

Copyright (c) 2006 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 16:04:04 ON 05 OCT 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

=> s quisqualate and prostate

L1 5 QUISQUALATE AND PROSTATE

=> dup rem l1

PROCESSING COMPLETED FOR L1

L2 2 DUP REM L1 (3 DUPLICATES REMOVED)

=> dis ibib abs

L2 ANSWER 1 OF 2 MEDLINE on STN

ACCESSION NUMBER: 2001510071 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11557259

TITLE: Binding of the glutamate carboxypeptidase II (NAALADase)

inhibitor 2-PMPA to rat brain membranes.

AUTHOR: Tiffany C W; Cai N S; Rojas C; Slusher B S

CORPORATE SOURCE: Guilford Pharmaceuticals Inc., 6611 Tributary Street,

Baltimore, MD 21224, USA.

SOURCE: European journal of pharmacology, (2001 Sep 14) Vol. 427,

No. 2, pp. 91-6.

Journal code: 1254354. ISSN: 0014-2999.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200111

ENTRY DATE: Entered STN: 17 Sep 2001

Last Updated on STN: 5 Nov 2001 Entered Medline: 1 Nov 2001

2-Phosphonomethyl pentanedioic acid (2-PMPA) is a potent and selective inhibitor of glutamate carboxypeptidase II (NAALADase), and has shown robust neuroprotective activity in both in vitro and in vivo models of ischemia. In the brain, glutamate carboxypeptidase II (GCPII) (EC3.4.17.21) hydrolyzes the neuropeptide N-acetylaspartylglutamate (NAAG) to glutamate and N-acetylaspartate. We report the development and characterization of a [(3)H]2-PMPA binding assay. [(3)H]2-PMPA binding was dependent on protein concentration, saturable, and displaceable. The association (k(on)) and dissociation (k(off)) rate constants were 3x10(6) M(-1) s(-1) and 0.01 s(-1), respectively. The dissociation equilibrium constant (K(d)) determined from the ratio of the rate constants (K(d)=k(off)/k(on)) was 1 nM. Scatchard analysis revealed one binding site with K(d)=2 nM and B(max)=0.7 pmol/mg. Binding exhibited similar pharmacological properties to GCPII enzyme activity, including chloride dependency, cobalt stimulation and inhibition by phosphate and

quisqualate. The binding of [(3)H]2-PMPA also showed tissue specificity in that tissues previously reported to be devoid of GCPII enzymatic activity were devoid of [(3)H]2-PMPA binding. [(3)H]2-PMPA binding represents an additional probe for the study of GCPII activity, and may be useful as a high throughput screening assay.

## => dis ibib abs 12 2

L2 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 1998041505 MEDLINE DOCUMENT NUMBER: PubMed ID: 9375657

TITLE: Molecular cloning of a peptidase against

N-acetylaspartylglutamate from a rat hippocampal cDNA

library

AUTHOR: Bzdega T; Turi T; Wroblewska B; She D; Chung H S; Kim H;

Neale J H

CORPORATE SOURCE: Department of Biology, Georgetown University, Washington,

D.C. 20057-1229, U.S.A.

SOURCE: Journal of neurochemistry, (1997 Dec) Vol. 69, No. 6, pp.

2270-7.

Journal code: 2985190R. ISSN: 0022-3042.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals OTHER SOURCE: GENBANK-U75973

ENTRY MONTH: 199712

ENTRY DATE: Entered STN: 9 Jan 1998

Last Updated on STN: 3 Mar 2000 Entered Medline: 12 Dec 1997

N-Acetylaspartylglutamate (NAAG) is the most prevalent peptide AB neurotransmitter in the mammalian nervous system. NAAG selectively activates the type 3 metabotropic glutamate receptor. It is inactivated by peptidase activity on the extracellular face of the plasma membrane of neurons and glia. The human gene that codes for prostate -specific membrane antigen (PSM) has been shown to produce peptidase activity against NAAG. We cloned the human PSM cDNA and used it to probe a rat hippocampal cDNA library. We identified a cDNA containing a complete coding region that possesses 83% homology with the PSM gene. The predicted 752-amino acid sequence has 85% identity and 91% similarity to the PSM sequence. CHO cells transfected with this cDNA expressed NAAG peptidase activity at a level similar to that obtained from rat brain membranes. The peptidase activity was inhibited by beta-NAAG, quisqualate, and pteroylglutamate but not aspartylglutamate or pteroic acid. In situ hybridization data demonstrated the widespread distribution of the peptidase mRNA in the brain, consistent with the distribution of peptidase activity. The highest levels of hybridization were detected in the hippocampus, dentate gyrus, piriform cortex, choroid plexus of the ventricles, pineal gland, anterior pituitary, and supraoptic nucleus. Three transcripts (estimated at 5, 3.4, and 2.9 kb) were identified in northern blots of rat brain, while in rat kidney the third transcript appeared slightly smaller than 2.9 kb. With use of reverse transcriptase PCR with primers for the 5' end, the central region, and the 3' end of the hippocampal cDNA, the expected amplification products were obtained from rat brain RNA. Spinal cord yielded an amplification product only with primers for the 5' end of the hippocampal cDNA.

Welcome to STN International! Enter x:x

LOGINID: ssptacmb1647

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

```
Web Page URLs for STN Seminar Schedule - N. America
NEWS
                 "Ask CAS" for self-help around the clock
NEWS
                New STN AnaVist pricing effective March 1, 2006
        FEB 27
NEWS
                CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS 4
        MAY 10
        MAY 11 KOREAPAT updates resume
NEWS 5
                Derwent World Patents Index to be reloaded and enhanced
        MAY 19
NEWS
                 IPC 8 Rolled-up Core codes added to CA/CAplus and
        MAY 30
NEWS
                 USPATFULL/USPAT2
                 The F-Term thesaurus is now available in CA/CAplus
NEWS
         MAY 30
                 The first reclassification of IPC codes now complete in
NEWS
         JUN 02
                 INPADOC
                 TULSA/TULSA2 reloaded and enhanced with new search and
NEWS 10
         JUN 26
                 and display fields
                 Price changes in full-text patent databases EPFULL and PCTFULL
NEWS 11
        JUN 28
                 CHEMSAFE reloaded and enhanced
NEWS 12 JUL 11
                 FSTA enhanced with Japanese patents
NEWS 13 JUl 14
                 Coverage of Research Disclosure reinstated in DWPI
NEWS 14 JUl 19
NEWS 15 AUG 09
                 INSPEC enhanced with 1898-1968 archive
NEWS 16 AUG 28
                 ADISCTI Reloaded and Enhanced
                 CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 17
        AUG 30
                 CA/CAplus enhanced with more pre-1907 records
         SEP 11
NEWS 18
                 CA/CAplus fields enhanced with simultaneous left and right
         SEP 21
NEWS 19
                 truncation
                 CA(SM)/CAplus(SM) display of CA Lexicon enhanced
         SEP 25
NEWS 20
                 CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 21
         SEP 25
                 CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
         SEP 25
NEWS 22
                 CEABA-VTB classification code fields reloaded with new
NEWS 23
         SEP 28
                 classification scheme
```

NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

```
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8
NEWS X25 X.25 communication option no longer available
```

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

FILE 'HOME' ENTERED AT 16:08:01 ON 05 OCT 2006

=> file medline embase biosis caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL

ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 16:08:19 ON 05 OCT 2006

FILE 'EMBASE' ENTERED AT 16:08:19 ON 05 OCT 2006 Copyright (c) 2006 Elsevier B.V. All rights reserved.

FILE 'BIOSIS' ENTERED AT 16:08:19 ON 05 OCT 2006

Copyright (c) 2006 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 16:08:19 ON 05 OCT 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

=> s beta-NAAG and prostate

L1 8 BETA-NAAG AND PROSTATE

=> dup rem

ENTER L# LIST OR (END):11
PROCESSING COMPLETED FOR L1

L2 2 DUP REM L1 (6 DUPLICATES REMOVED)

=> dis ibib abs 12 1-2

L2 ANSWER 1 OF 2 MEDLINE ON STN DUPLICATE 1

ACCESSION NUMBER: 1998041505 MEDLINE DOCUMENT NUMBER: PubMed ID: 9375657

TITLE: Molecular cloning of a peptidase against

N-acetylaspartylglutamate from a rat hippocampal cDNA

library.

AUTHOR: Bzdega T; Turi T; Wroblewska B; She D; Chung H S; Kim H;

Neale J H

CORPORATE SOURCE: Department of Biology, Georgetown University, Washington,

D.C. 20057-1229, U.S.A.

SOURCE: Journal of neurochemistry, (1997 Dec) Vol. 69, No. 6, pp.

2270-7.

Journal code: 2985190R. ISSN: 0022-3042.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE).

LANGUAGE: English

FILE SEGMENT: Priority Journals OTHER SOURCE: GENBANK-U75973

ENTRY MONTH: 199712

ENTRY DATE: Entered STN: 9 Jan 1998

Last Updated on STN: 3 Mar 2000 Entered Medline: 12 Dec 1997

AB N-Acetylaspartylglutamate (NAAG) is the most prevalent peptide neurotransmitter in the mammalian nervous system. NAAG selectively activates the type 3 metabotropic glutamate receptor. It is inactivated by peptidase activity on the extracellular face of the plasma membrane of neurons and glia. The human gene that codes for prostate -specific membrane antigen (PSM) has been shown to produce peptidase activity against NAAG. We cloned the human PSM cDNA and used it to probe a rat hippocampal cDNA library. We identified a cDNA containing a complete coding region that possesses 83% homology with the PSM gene. The predicted 752-amino acid sequence has 85% identity and 91% similarity to the PSM sequence. CHO cells transfected with this cDNA expressed NAAG

peptidase activity at a level similar to that obtained from rat brain membranes. The peptidase activity was inhibited by beta-NAAG, quisqualate, and pteroylglutamate but not aspartylglutamate or pteroic acid. In situ hybridization data demonstrated the widespread distribution of the peptidase mRNA in the brain, consistent with the distribution of peptidase activity. The highest levels of hybridization were detected in the hippocampus, dentate gyrus, piriform cortex, choroid plexus of the ventricles, pineal gland, anterior pituitary, and supraoptic nucleus. Three transcripts (estimated at 5, 3.4, and 2.9 kb) were identified in northern blots of rat brain, while in rat kidney the third transcript appeared slightly smaller than 2.9 kb. With use of reverse transcriptase PCR with primers for the 5' end, the central region, and the 3' end of the hippocampal cDNA, the expected amplification products were obtained from rat brain RNA. Spinal cord yielded an amplification product only with primers for the 5' end of the hippocampal cDNA.

L2 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 96149377 MEDLINE DOCUMENT NUMBER: PubMed ID: 8570628

TITLE: Prostate-specific membrane antigen is a hydrolase

with substrate and pharmacologic characteristics of a

neuropeptidase.

AUTHOR: Carter R E; Feldman A R; Coyle J T

CORPORATE SOURCE: Department of Psychiatry, Massachusetts General

Hospital-East, Charlestown 02129, USA.

CONTRACT NUMBER: MH-572901 (NIMH)

SOURCE: Proceedings of the National Academy of Sciences of the

United States of America, (1996 Jan 23) Vol. 93, No. 2, pp.

749-53.

Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals OTHER SOURCE: GENBANK-AF039707

ENTRY MONTH: 199603

ENTRY DATE: Entered STN: 15 Mar 1996

Last Updated on STN: 3 Mar 2000 Entered Medline: 1 Mar 1996

This report demonstrates that the investigational prostatic carcinoma AB marker known as the prostate-specific membrane antigen (PSM) possesses hydrolytic activity with the substrate and pharmacologic properties of the N-acetylated alpha-linked acidic dipeptidase (NAALADase). NAALADase is a membrane hydrolase that has been characterized in the mammalian nervous system on the basis of its catabolism of the neuropeptide N-acetylaspartylglutamate (NAAG) to yield glutamate and N-acetylaspartate and that has been hypothesized to influence glutamatergic signaling processes. The immunoscreening of a rat brain cDNA expression library with anti-NAALADase antisera identified a 1428-base partial cDNA that shares 86% sequence identity with 1428 bases of the human PSM cDNA [Israeli, R. S., Powell, C. T., Fair, W. R. & Heston, W.D.W. (1993) Cancer Res. 53, 227-230]. A cDNA containing the entire PSM open reading frame was subsequently isolated by reverse transcription-PCR from the PSM-positive prostate carcinoma cell line LNCaP. Transient transfection of this cDNA into two NAALADase-negative cell lines conferred NAAG-hydrolyzing activity that was inhibited by the NAALADase inhibitors quisqualic acid and beta-NAAG. Thus we demonstrate a PSM-encoded function and identify a NAALADase-encoding cDNA. Northern analyses identify at least six transcripts that are variably expressed in NAALADase-positive but not in NAALADase-negative rat tissues and human cell lines; therefore, PSM and/or related molecular species appear to account for NAAG hydrolysis in the nervous system. These results also raise questions about the role of PSM in both normal and pathologic prostate epithelial-cell function.

=> FIL STNGUIDE COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY 9.44 SESSION 9.65

FULL ESTIMATED COST

FILE 'STNGUIDE' ENTERED AT 16:10:21 ON 05 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Oct 4, 2006 (20061004/UP).